DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-281/S-030
NDA 21-123/S-001

Ortho-McNeil Pharmaceutical, Inc.
Attention: Robyn Keown
Manager, Regulatory Affairs
1000 U.S. Highway
P.O. Box 300
Raritan, NJ 08869-0602

Dear Ms. Keown:

Please refer to your supplemental new drug applications, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, dated October 15, 2003, received October 16, 2003, for Ultram® (tramadol hydrochloride) Tablets 100 mg, 50 mg and Ultracet® (325 mg acetaminophen/37.5mg tramadol hydrochloride) Tablets.

These supplemental new drug applications provide for amending the Ultram® and Ultracet package inserts by expanding terms describing very rare discontinuation symptoms that have bee reported through surveillance and clinical monitoring programs.

We completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the submitted labeling package insert submitted April 14, 2004.

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 20-281/S-030 and NDA 21-123/S-001." Approval of these submissions by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Barbara Gould, Regulatory Project Manager, at (301) 827-2506.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Sharon Hertz

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